Dermatology Practical & Conceptual

Significant Nevi Regression Associated with Multiple Non-Metastatic Cutaneous Melanomas: A Case Report

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Introduction

Spontaneous regression in melanocytic nevi in patients with a personal history of melanoma is a rare and intriguing phenomenon [1]. We present an extremely rare case of a patient with a history of multiple non-metastatic melanomas and dysplastic nevi syndrome who subsequently experienced sudden regression of nearly all nevi.

Case Presentation

A 73-year-old male patient with dysplastic nevi syndrome has been under follow-up at our Department for more than two decades. In 1993, he was diagnosed with an intermediate-thickness melanoma in the right temporal region. Melanoma *in situ* was excised from the left abdominal area in 2013, followed by the removal of a superficial spreading melanoma (SSM) (Clark II, Breslow thickness 0.32 mm) from his back in 2014. In August 2023, a superficial atypical melanocytic proliferation of uncertain significance (SAMPUS) was excised from his left upper arm. At the beginning of 2023, signs of initial regression in multiple nevi were observed upon digital dermoscopy. Surprisingly, by September 2023, a routine total body photography follow-up revealed the remarkable disappearance of almost all nevi (Figure 1). At the same time, an SSM was excised from the patient's back (Clark II, Breslow thickness of 0.56 mm).

Three regressed nevi were removed and showed dysplastic nevi with halo-type inflammatory reaction (Figure 2). The patient's only current medication was tamsulosin, prescribed for benign prostatic hyperplasia. Given the notable dermoscopic findings of regressed nevi and the newly identified melanoma, a PET-CT scan was conducted, which revealed no pathological metabolic activity

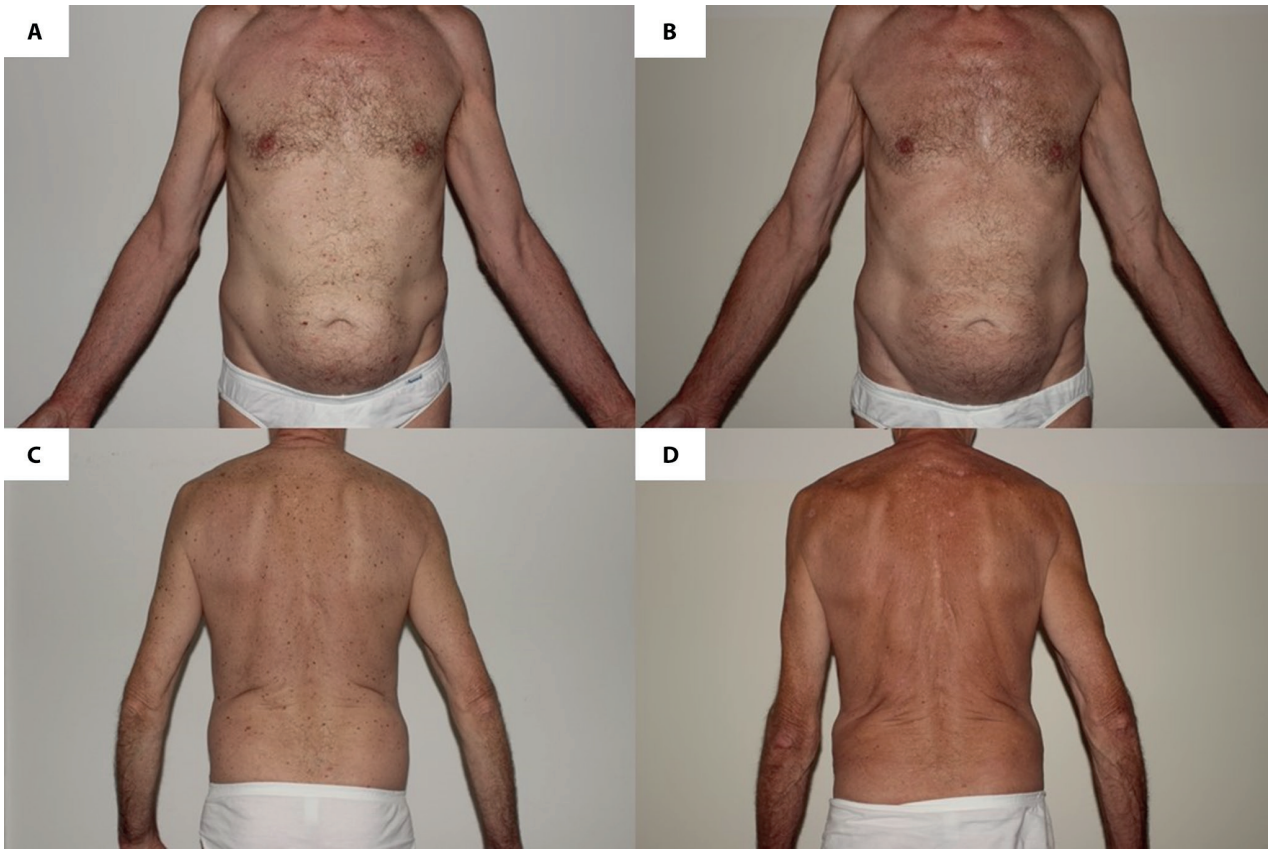

Figure 1. Clinical presentation before (a, c) and after (b, d) spontaneous regression of dysplastic nevi on the patient's trunk.

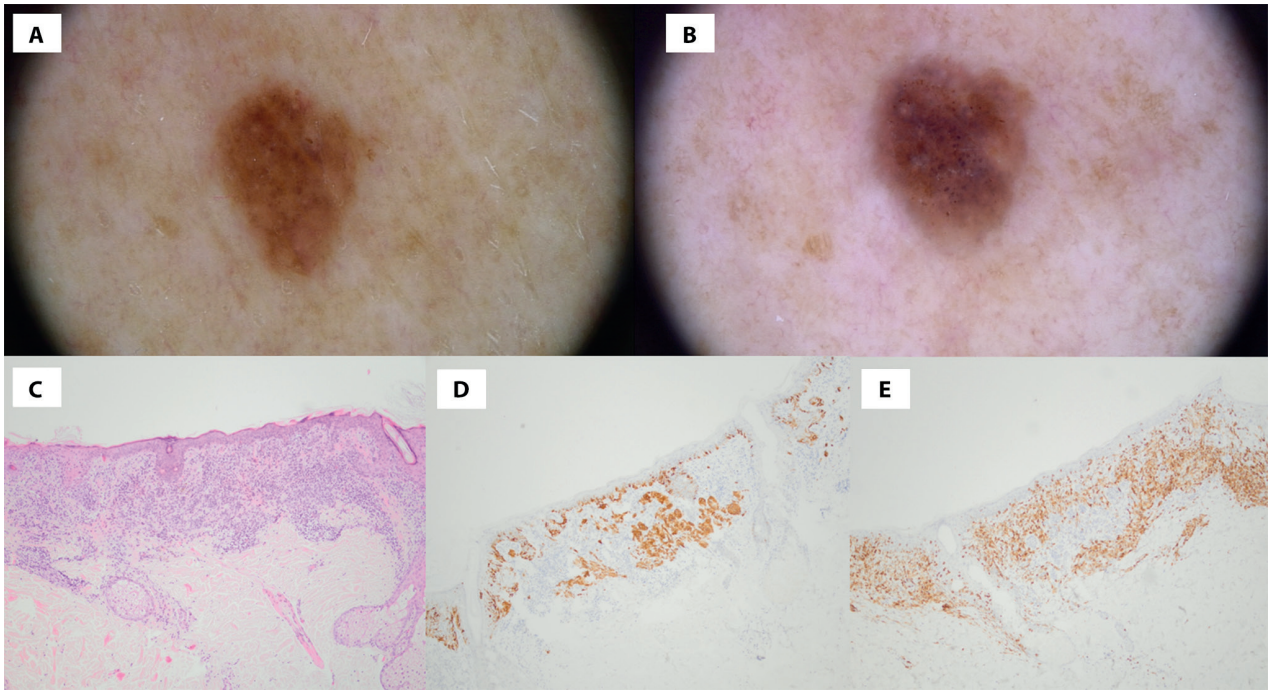

Figure 2. (a) Dermoscopic image of one of the three dysplastic nevi, taken on 21 October 2016. (b) Dermoscopic image of the same nevus, taken on 12 December 2022. Regression is clearly visible. (c) Histologic image of dysplastic nevus on the patient' back (hematoxylin-eosin; 100x). "Halo" type of inflammation indicates early regression. (d) Melan-A staining of the same nevus (x100). (e) CD45 staining, which is specific for lymphocytes, reveals a significant inflammation at the base of the nevus and between the nevus cells in the dermis (x100).

of fluorodeoxyglucose. Additionally, S100 and LDH levels were within normal ranges; thus, there was no indication of an active malignant disease.

Conclusions

Nevus regression in melanoma patients is predominantly driven by immune-mediated mechanisms targeting melanocytes. Melanocytes and melanoma cells share melanocyte differentiation antigens (MDAs) such as MART-1, gp100, and tyrosinase, which are recognized by the immune system. Cytotoxic T lymphocytes (CTLs) are critical in melanocyte destruction by recognizing tumor-associated antigens presented on MHC class I molecules and inducing apoptosis. Additionally, immune checkpoints such as PD-1/PD-L1 and CTLA-4 regulate immune responses but can be exploited by melanoma cells to evade the immune system [2]. Therefore, it is not surprising that the regression of nevi and vitiligo-like depigmentation has been reported in patients with metastatic melanoma, which has been explained by an increased antigen load as melanoma progresses to metastatic disease [3].

Our patient experienced spontaneous regression of nearly all nevi without a diagnosis of metastatic melanoma or receiving immunotherapy, which is an exceptionally rare event since it has been reported in the literature in only three patients [1,4,5]. The explanation for the spontaneous regression of nevi in our patient may lie in the fact that he had dysplastic nevus syndrome, since dysplastic nevi, in comparison with melanocytic nevi, may exhibit higher levels of MDAs, which are also expressed by melanoma cells. This heightened expression and increased production of lymphocyte-recruiting chemokines and adhesion molecules may attract more tumor-infiltrating lymphocytes [4]. Further research is necessary to enhance our understanding of this phenomenon.

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